Evaluate Vantage

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# Snippet roundup: A bad week for Bristol and Adocia

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Welcome to your weekly roundup of EP Vantage's snippets – short takes on smaller news items.

This week, January 23-27, 2017, we had thoughts on the following: Lilly dumps Adocia again; Bristol sinks as it kitchen-sinks; Eisai to muscle in on Bayer's liver cancer franchise; J&J provides restrained start to earnings season; Actelion's Maestro hits flat note.

These snippets were previously published daily via twitter.

**Lilly dumps Adocia again**

**January 27, 2017**

For the second time, Lilly has taken a look at data from Adocia's ultrafast version of Humalog and decided to stick with its own internal project. The French biotech will now assume control of Biochaperone Lispro U100, and will need to try to lure a new partner on the basis of data from an insulin pump trial reported in December. Lilly has thrown a total of $60m in up-front cash – and probably some milestones that were not disclosed – at Adocia over the course of two separate licences, which have run in parallel to the Indiana big pharma's work on its own ultra-rapid insulin. Both are well behind Novo Nordisk's Fiasp, which was approved in Europe earlier this month and awaits a resubmission to the US FDA. With insulin becoming an increasingly competitive and price-sensitive space, Lilly and Adocia will need to fight hard to show how their new ultrafast projects are differentiated from Fiasp. And, after its diabetic foot ulcer project failed in clinical trials last year, Adocia is heavily exposed to insulin pressures. Shares fell 31% in early trading today.

**Adocia pipeline**

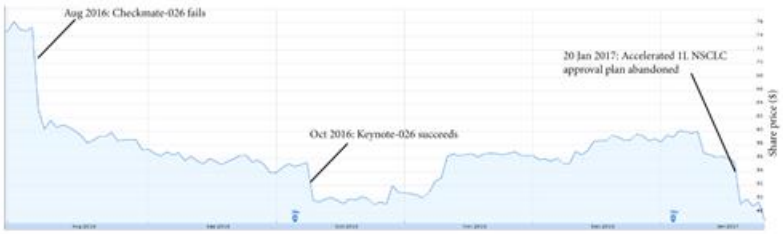
| Product | Pharmacological Class |
|---|---|
| **Phase II** | |
| BioChaperone Lispro U100 | Insulin analogue |
| BioChaperone Lispro U200 | Insulin analogue |
| HinsBet U100 | Insulin |
| BioChaperone Combo | Insulin |

*Source: EvaluatePharma*

**Bristol sinks as it kitchen-sinks**

**January 27, 2017**

Perhaps the most astonishing admission on Bristol-Myers Squibb's full-year analyst call yesterday was that the group now assumed that Merck & Co would get US approval for Keytruda plus chemotherapy in first-line lung cancer, based on the Keynote-021 trial. It is hard not to see this as an admission of defeat, since it is by no means certain that Keynote-021 – an uncontrolled trial that failed to extend overall survival – can support approval. It did not help that Bristol's management was unwilling to shed any light on its own strategy in this setting since abandoning an accelerated plan based on the Checkmate-568 trial, implying that it would simply hope for the best with the controlled Checkmate-227 study, due to yield data in PD-L1 expressers in early 2018, and from expanded arms later; earlier interim analyses are possible, but the strong suggestion is that Bristol has seen Checkmate-568 data, and that these have disappointed. Bristol's day of setbacks went from bad to worse, with forecasts missed and 2017 guidance cut, and even extended to poor sound quality on the analyst call that it felt necessary to deny as being an attempt to "muffle conversation". The stock fell almost 6%.




$BMY share price

**Eisai to muscle in on Bayer's liver cancer franchise**

**January 25, 2017**

After more than a decade where Bayer's Nexavar has been its only approved therapy, hepatocellular carcinoma looks set to see new choices emerge this year. Today Eisai said Lenvima met its primary endpoint of showing non-inferiority to the incumbent in a large phase III study; exact details have yet to be revealed, though Nexavar was approved on the basis of a 2.8-month extension in overall survival to 10.7 months (HR=0.69). Nexavar is a very toxic drug so the relative tolerability profiles of the two multi-kinase inhibitors will be important – Lenvima could offer the potential to combine this mechanism with other agents, such as checkpoint inhibitors. As it happens, full data on Lenvima could emerge at Asco, around the time Bristol-Myers Squibb's phase III Checkmate-459 study of Opdivo in the first-line setting; early data suggest that the checkpoint inhibitor confers a durable response in around 20% of HCC patients. Investors should watch carefully for any move by Bayer to shore up its position by studying Stivarga, its newer kinase inhibitor that should shortly be approved in second-line HCC, in the first-line setting. But it will surely have to see data on Lenvima and Opdivo before doing so.

**Phase III trials in first line advanced hepatocellular carcinoma**

| Project | Company | Trial Name | n | Trial Design | ID | Data |
|---|---|---|---|---|---|---|
| Lenvima | Eisai | - | 954 | vs Nexavar | NCT01761266 | Jan-17 |
| Opdivo | BMS | CheckMate 459 | 726 | vs Nexavar | NCT02576509 | May-17 |
| Livatag | Onxeo | Relive | 390 | vs BSC | NCT01655693 | Jul-17 |
| Pexa-Vec | Sillagen | Phocus | 600 | Nexavar +/- | NCT02562755 | Oct-17 |
| Therasphere | BTG | Yes-P | 328 | vs Nexavar | NCT01887717 | Jun-19 |
| Therasphere | BTG | Stop-HCC | 390 | Nexavar +/- | NCT01556490 | Jul-19 |

**J&J provides restrained start to earnings season**

**January 24, 2017**

Johnson & Johnson has kicked off the pharma earnings season with disappointing fourth-quarter results and, perhaps more worryingly, cautious guidance for this year. Anyone expecting things to start getting better for the industry might have to wait a bit longer – the news sent J&J's stock down 2% this morning and also had a negative impact on broader pharma indices. The group's chief financial officer, Dominic Caruso, admitted that sales growth in its pharma business would slow in 2017 versus 2016, which he put down to currency effects and an ageing stable of products – and this is without taking into account the impact of the Remicade biosimilar Inflectra. The company needs an acquisition to spur future growth, but refused to comment about the long-awaited takeout of Actelion. J&J executives seem more keen on smaller bolt-on buys rather than a big, transformative acquisition, with chief exec Alex Gorsky saying the latter are more focused on cost-cutting and synergies and would not bring the growth and innovation it is looking for. Meanwhile, J&J is also considering selling its diabetes device businesses, Lifescan, Animas and Calibra Medical, citing a harsh pricing environment.

**Actelion's Maestro hits flat note**

**January 23, 2017**

The failure of a label-expansion trial of Actelion's pulmonary arterial hypertension therapy Opsumit was not enough to put off investors – they pushed its share price up 3% this morning, seemingly optimistic that the setback would not hit the long-rumoured acquisition by Johnson & Johnson. True, the Maestro study was in the small indication of Eisenmenger syndrome, so the stumble probably has a minimal impact on Opsumit's 2022 consensus sales forecast of $1.6bn. Even so, label expansion is one key to bolstering the product's future sales, and the failure could help J&J's negotiating efforts – particularly if it is only interested in Actelion's marketed products rather than its pipeline, as speculated. The rumoured $28bn price tag already looks rich compared with Actelion's NPV of $7.2bn – or $6.6bn if only approved products are included. The Swiss group will hope for better luck with its other label-expansion efforts for Opsumit, to add to earlier success in the Merit study in inoperable chronic thromboembolic pulmonary hypertension.

**Selected ongoing phase III/IV trials of Opsumit**

| Trial | Indication | ID | Primary completion |
|---|---|---|---|
| Portico | Portopulmonary hypertension | NCT02382016 | Jul-17 |
| Optima | Combination of Opsumit and tadalafil in newly diagnosed PAH | NCT02968901 | Nov-17 |
| Repair | Right ventricular remodelling in PAH | NCT02310672 | Dec-17 |
| Triton | Triple combo of Opsumit, Uptravi and tadalafil versus Opsumit and tadalafil in newly diagnosed PAH | NCT02558231 | Dec-18 |
| Tomorrow | Paediatric PAH | NCT02932410 | Jul-22 |

*Source: EvaluatePharma*

Since these snippets were published J&J has agreed to acquire Actelion for $30bn: *J&J sets benchmark with massive Actelion price, January 26, 2017*.

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